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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,940	11/26/2003	Sherry Leonard	VARD-07989	4237

7590 06/06/2006

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,940	LEONARD ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7-21 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I (claims1-6 &22-25) in the reply filed on 3/14/06 is acknowledged. The traversal is on the ground(s) that Groups I and II are overlapping. This is found to be persuasive. Claims 1-8, and 22-25 are under examination.

The remainder of the requirement is still deemed proper and is therefore made FINAL.

Priority

It is noted the instant application is a continuation in part of 08/956,518, now us patent number 6,875,606. However the examiner can find no basis in the earlier specification for an assay to identify polymorphisms within the alpha-7 receptor promoter region (recited in claims 2-3) and correlate them with predisposition for schizophrenia. Therefore the examiner asserts that the instant claims related to specific polymorphisms in the promoter region only merit the priority of the instant application, which is 11/26/03. If applicant believes otherwise, it is suggested that applicant point out by page and line in the '518 specification where support for the instant claims can be found.

IDS

References 190 and 191 have been considered. However, in the absence of an alignment with a sequence of the instant application, the examiner cannot assess the relevance of the references.

Claim 1 is objected to because of the following informalities: there should be a 'to' between 'predisposed' and 'schizophrenia.' Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method to identify individuals predisposed to schizophrenia by correlating the presence of a polymorphism in the alpha-7 nicotinic

receptor allele with a predisposition to schizophrenia. The method further recites diagnosis and differential diagnosis in claims 7 and 8. The method is complex because reciting "polymorphisms within said alpha-7 allele" other than the ones disclosed in the specification are not predictable and are completely unknown without undue further experimentation. It is also not predictable whether or not a generic variant of the alpha-7 allele will mark a predisposition to schizophrenia. Also, with respect to diagnosis and differential diagnosis of schizophrenia the invention is complex because diagnosis would involve multiple genes and environmental factors that are currently not taught.

The state of the art at the time of filing is that there is ***no way to genetically diagnose schizophrenia*** and that linkage analysis has suggested that there are multiple genes with small effects and incomplete penetrance (see abstract and page 28, right col top, Miyamoto et al., 2003). Further, the art does not teach all variants of the alpha-7 nicotinic receptor allele and does not teach that every allelic variant or polymorphism is related to schizophrenia.

The level of predictability of the art is low. In particular, the specification identifies some promoter variants that decrease expression of the alpha-7 receptor, but any newly discovered polymorphism would not necessarily result in effects on the receptor expression or function. Therefore the predictability of the relationship between schizophrenia and polymorphisms of the alpha-7 gene is very low. Also, since there is currently NO method of genetic diagnosis of schizophrenia the predictability of a genetic diagnostic for schizophrenia is nil.

There are no working examples that diagnose schizophrenia by obtaining and genotyping an alpha-7 allele in a patient. There are also no examples that teach that every variation in the alpha-7 allele is predictive of predisposition or is diagnostic for schizophrenia. There is no guidance in the specification as to how to make a genetic diagnosis of schizophrenia with the current method. There is also no guidance as to how to recognize a polymorphism in the alpha-7 allele without undue experimentation.

Therefore, because of the complex nature of the invention, the lack of predictability of the art, the contrasting teachings in the art, and the lack of guidance or example in the specification, it would require one of skill in the art undue experimentation to make or use the invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 and 22 are vague and indefinite in so far as they employ terms such as 'α-7 allele' or '-241 A to G' as limitations without reference to precise nucleic acid sequences. Without identification of property or combination of properties which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Claims 4-6 and 23-24 are rejected for depending on indefinite claims.

Claims 7 and 8 are indefinite because they recite diagnosis but it is not clear ***what they diagnose***. Further, the method cannot simultaneously indicate a predisposition and indicate a diagnosis of the disease. They do one or the other.

Claims 1-6, and 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a method wherein the conditions for identifying are either met or not. For example, claim 1, 'step c) correlating...wherein a polymorphism that is found in schizophrenics significantly more often than controls is a polymorphism that predisposes an individual to schizophrenia.' Claim 22 lacks a final step also. Claims 2-6 and 22-24 are rejected for depending on claims 1 and 22.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 5, 6, and 22-24 rejected under 35 U.S.C. 102(b) as being anticipated by Freedman et al. (1997).

Freedman et al recite providing nucleic acids from control and schizophrenic subjects (see methods, page 588) to link a polymorphism (S15S1360) near exon 2 in the alpha-7 allele a high P50 ratio, which is an auditory deficit, linked to schizophrenia

(see figure 1, page 588). Therefore, Freedman et al meets the limitations of claims 1 and 22 because subjects provided nucleic acid samples, an polymorphism in the alpha-7 allele was detected, and the polymorphism 'S15S1360' was correlated with high P50 ratios and with schizophrenia. Freedman et al uses PCR (see page 589, left col) which meets the limitations of claims 5 and 23. A blood sample was used in Freedman et al (see page 589 under 'isolation of polymorphisms') which meets the limitations of claims 6 and 24.

Claims 2-6 and 23-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Leonard et al (December, 2002).

Leonard et al describe a method comprising obtaining a sample comprising the alpha7 allele from postmortem brain (page 1087), detecting the presence of at least one polymorphism by sequencing (see methods, page 1085), and correlating the presence of said at least one polymorphism with a predisposition to schizophrenia (see results, page 1085), which meets the limitations of claims 1, 5-6, and 22-24. Leonard et al identify polymorphisms that reduce alpha-7 receptor expression (see figure 3, page 1092) which meets the limitations of claim 4. While it is not entirely clear whether the '-241 A to G' and '-194 G to C' of Leonard et al are the same as the polymorphisms of the instant application, absent evidence to the contrary, Leonard et al disclosed the polymorphisms recited in claims 2-3 in the promoter region of alpha-7 receptor. Thus, Leonard et al meet the limitations of claims 2-3. Leonard et al does not meet the

limitations of claims 1 and 22 because Leonard et al does not constitute prior art to those claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LORRAINE SPECTOR
PRIMARY EXAMINER

Steve Standley, Ph.D.
5/22/06